plasma folate (8.9±3.8 to 34.3±16.5μg/l & 9.9±4.1 to 17.4±7.6μg/l respectively; Δ high c.f. low dose p<0.001). Both doses of folic acid significantly (p<0.001) lowered plasma total homocysteine (12.9±5.6 to 9.9±2.6μmol/l for high dose & 11.7±3.1 to 10.5±1.8μmol/l for low dose; Δ high c.f. low dose p=0.219). However, FMD was improved only following high (99±35 c.f. 24±26μm pretreatment, p<0.001) and not low (42±32 c.f. 26±59μm pretreatment, p=0.264) dose folic acid. No differences between groups were evident for any of the other parameters measured.
Conclusion: The data demonstrate that high but not low dose folic acid improves endothelial function in CAD despite a significant reduction in homocysteine in both treatment groups. This suggests that the beneficial effects of folic acid on endothelial function occur via a mechanism that is independent of homocysteine-lowering. These results have important implications for the current clinical trials of folic acid supplementation using low dose folic acid.

1159-187 Long-Term Use of Pioglitazone Slows Arteriosclerotic Progression in Type 2 Diabetics

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Introduction and hypothesis: Insulin resistance is thought to be highly involved in arteriosclerotic processes, but the long-term effects of insulin sensitizing agents remain unknown. We assessed hypothesis that long-term use of pioglitazone, an insulin sensitizer, slows ultrasonic manifestation of atherosclerosis.
Methods: Thirty type-2 diabetic patients with suspected coronary artery disease were randomized to group-P where they received pioglitazone (30mg per day) for more than 1 year, or to group-C where they continued therapy without thiazolidinedione for more than 1 year. We noninvasively ultrasonic quantified flow mediated dilation of brachial artery after 5 minutes forearm occlusion (FMD) and we also quantified arterial stiffness by brachial-to-ankle pulse wave velocity (PWV). Changes in FMD and PWV from the baseline through the follow-up point were compared between the 2 groups. **Results:** Group-P (n=15) manifested good compliance to the treatment and improvements in insulin resistant variables represented by HOMA-IR while group-C showed no improvement. FMD was improved after medication in group-P (p<0.01) but not in group-C (p=ns). PWV decreased in group-P (p=0.02) but increased in group-C (p=0.03).
Conclusion: In conclusion long-term pioglitazone use improves endothelial function and arterial wall compliance, which may have beneficial potentials for management of arteriosclerosis in type-2 diabetics.

	Baseline group-P	Follow-up group-P	Baseline group-C	Follow-up group-C
FMD	4.1±1.6%	7.1±2.7%	1727±269cm/s	1664±234cm/s
PWV	4.1±1.8%	4.2±1.7%	1710±232cm/s	1797±215cm/s

1159-188 Grape Seed and Skin Extracts Alter Platelet Function and Release of Reactive Oxygen Species

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Background: Moderate red wine consumption is inversely associated with coronary ischemia. Red wine and purple grape juice (PGJ) contain polymeric flavonoids with antioxidant properties believed to be protective against cardiovascular events. Acute cardiac events are also associated with decreased platelet-derived nitric oxide (NO) release. In this study, the effects of extracts from grape skins or seeds on platelet function, NO, and superoxide release were determined.
Methods and Results: Incubation of platelets with seed (100 mg/L) or skin (250 mg/L) extract led a decrease in platelet aggregation of 65% ± 7% and 49% ± 9%, respectively (n=6; P<0.001). Grape seed or skin extract increased platelet-derived NO release by 126% ± 19% and 92% ± 20%, respectively (n=5, P<0.001). Platelet incubation with extracts led to a marked decrease in superoxide release from 73 ± 6 to 2 ± 3 for grape seeds and to 7.3 ± 6.4 for grape skin (arb. Chemilum. units; n=5, P<0.0001). These effects were dose-dependent for both grape extracts. Coincubation with seeds and skins led to additive effect on inhibition of platelet aggregation, enhanced NO release, and ablated superoxide production, but did not significantly alter release of aggregation induced soluble CD40 ligand, a marker of inflammatory-thrombotic interactions.
Conclusion: The skins and seeds from grapes inhibit platelet function and increase bioactive NO. These effects may be due to the markedly decreased release of superoxide anion or via another antioxidant-sparing mechanism. Red wine has been shown to enhance vascular function via a NO-dependent mechanism and the extracts derived from grapes appear to provide similar beneficial properties.

1159-189 Echocardiographic Correlates of Pulmonary Hypertension in 2,337 Patients

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Background: Echocardiographic findings in a large population of unselected patients with pulmonary hypertension (PH) have not been reported, and are herein described.
Methods: Using our echocardiographic database, we retrospectively identified all adult patients having measurable tricuspid regurgitation (n=14,869). Patients with estimated RV-RA gradients _ 40 mmHg were defined as having PH (n=2,337); those having gradients _ 20 were defined as having no PH (n=3,136). Demographic information, clinical data and codified echocardiographic findings were analyzed for their association with PH. Differences between cohorts were assessed using the t-test and chi square test for continuous and dichotomous variables, respectively.
Results: The PH cohort was significantly older (64.3±16.9 yrs vs. 47.1 ± 17.7 yrs) and had a small but significant male preponderance (50.3% vs. 45.2%). Body mass index (BMI) was significantly greater in the PH group (30.2 ± 10.2 vs. 27.3± 7.3), and grouped analyses of echocardiographic parameters are presented below.
Conclusion: PH was present in over 15% of patients with measurable tricuspid regurgitation. Compared to patients without PH, there are striking differences in age, sex, weight and measures of atrial, LV, RV and valvular morphology and function. A significant number of PH patients (25.3%) lacked left-sided pathology that could contribute to the presence of PH. To our knowledge, this study represents the largest cohort of unselected PH patients described.

Clinical and Echocardiographic Findings	Pulmonary Hypertension (n=2,337)	No Pulmonary Hypertension (n=3,136)	p-value
Age in years (mean ± SD)	64.3 ± 16.9	47.1 ± 17.7	<.001
Gender Female (%)	49.7%	54.8%	<.001
BMI (Kg/m^2, mean ± SD)	30.2 ± 10.2	27.3 ± 7.3	<.001
Abnormal LV Morphology or Function	69.4%	30.6%	<.001
Abnormal RV Morphology or Function	35.9%	11.3%	<.001
Abnormal Atrial Morphology or Rhythm	58.0%	23.3%	<.001
Moderate or Severe Left Sided Valvular Disease	35.0%	7.8%	<.001
Pericardial Abnormalities	20.5%	9.5%	<.001
Any L-Sided Abnormalities (Valvular, Structural or Functional)	74.7%	41.0%	<.001

1159-190 Role of the 807 C/T Polymorphism of Glycoprotein Ia/IIa on Platelet Function Following Clopidogrel Loading Dose in Patients Undergoing Coronary Stenting

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Background: The 807 C/T polymorphism of the glycoprotein (GP) Ia/IIa is the major platelet-collagen receptor. In particular, T allele carriers have increased receptor density and thrombotic risk. Aim of the study was to assess the role of the 807 C/T polymorphism on platelet aggregation (PA) following a 300 mg clopidogrel loading dose (LD) after coronary stenting (CS). **Methods:** The 807 C/T genotype was assessed in 44 patients (P). P were divided into 2 groups: carriers (CT + TT genotypes) and non-carriers (CC genotype) of the T allele. All P were on aspirin and those receiving GP IIb/IIIa blockers were not included. PA (expressed as %) was assessed at baseline (B), and 4hrs and 24hrs following LD by light transmittance aggregometry using ADP (6 μM) and collagen (6 μg/mL) as agonists. **Results:** There were 32/44 T allele carriers and 12/44 CC homozygotes. ADP-induced PA did not differ between groups (Table). Following collagen stimuli, PA was higher (*p<0.05) in T allele carries following LD (Table). PA reduced (#p<0.001) at 4 and 24 hrs in all P except after collagen stimuli in T allele carriers. There were no differences in fibrinogen and von Willebrand factor levels, platelet count, and clinical status. **Conclusions:** The T allele of the GP Ia/IIa gene is associated with increased platelet reactivity and a lower response to clopidogrel LD following collagen stimuli. This suggests that T allele carriers have a more extensive platelet adherence to fibrillar collagens which may contribute to their increased thrombotic risk.

ADP	**B**	**4 hrs**	**24 hrs**
CC	61±16	43±13#	32±9#
CT+TT	55±18	42±18#	35±19#
Collagen	**B**	**4 hrs**	**24 hrs**
CC	42±15	30±13#	31±14#
CT+TT	47±19	43±21*	46±26*

1159-191 Effect of a Single High-Fat Meal on Endothelial Microparticles as a Marker of Endothelial Injury

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BACKGROUND: This study was designed to evaluate a possible relationship between levels of CD31+/CD42b- Endothelial Microparticles (EMP), markers of endothelial injury, and cholesterol levels in healthy volunteers.
METHODS: A total of 23 healthy subjects without any major risk factors or previous cardiovascular risk factors were evaluated. A fasting cholesterol profile and EMP levels were measured in all subjects. Endothelial microparticles were measured by flow cytometry using fluorescent monoclonal antibodies.
RESULTS: Subjects were divided in two different groups according to fasting total cholesterol. Group A had cholesterol levels below 200 mg/dl (157 ± 31) and group B had serum cholesterol equal or greater than 200 mg/dl (258.4 ± 11.14); p: < 0.0001. The measured levels of EMP (x10^6/mL) were 0.388824 ± 0.053954 in group A and 0.964 ± 0.185148589 in group B (P< 0.0001). The 17 subjects in group A were then fed a high fat meal containing 900calories, 50g of fat, 14g of saturated fat, and 255mg of cholesterol. The measured levels of EMP (x10^6/mL) fasting, at one hour and three hours were 0.388824 ± 0.053954, 0.541176 ±0.138649 and 0.676667 ±0.158505, respectively.